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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,881	10/05/2005	Sander Jan Hendrik Van Deventer	28902.nob11	6763

1444 7590 08/09/2010

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EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
08/09/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,881	VAN DEVENTER ET AL.	
	Examiner	Art Unit	
	DANIEL C. GAMETT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,20,21 and 23* is/are pending in the application.

4a) Of the above claim(s) *10-17 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647. The Examiner for this Application is now Daniel C. Gamett, Ph.D.

1. The amendments of 06/23/2010 have been entered in full. Claims 18, 19, and 22 are cancelled. Claims 1-17, 20, 21 and 23 are pending. Claims 10-17 and 23 are withdrawn. Claims 1-9, 20, and 21 are under consideration.

2. All prior objection/rejections not specifically maintained in this office action are hereby withdrawn.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-9, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6540999, filed January 31, 1997, Takayama *et al.*, Transplantation. 2001 May 15;71(9):1334-1340, Setoguchi *et al.* (J. of Immunology, 165(10): 5980-5986, 2000, (of record) and Mavilio *et al.* (Blood, 83(7): 1988-1997, April 1, 1994, (of record).

5. The '999 patent teaches that stimulation of a variety of cell types, including human immune cells, T cells, macrophages, non-T, non-B splenic cells, cells from human allergy patients and cancer patients, even normal human peripheral blood mononuclear cells, with Lewis

antigen-containing conjugates results in the production of cytokines that regulate the development of Th1 or a Th2 response. The Lewis antigen-containing conjugates were shown to stimulate production of a variety of Th2-associated cytokines, including IL-10, IL-4 and IL-5. This stimulated cytokine production is taught to be useful for modulating immune responses (paragraph bridging columns 2-3). The variety of responding cells indicates that, even though the stimulant is named "Lewis antigen" the disclosed response is not "antigen specific" as it could not be mediated by a specific antigen receptor such as a TCR or antibody. ("Lewis antigen" denotes a chemical structure; it is not functioning as an antigen in this instance.) Thus, the '999 patent teaches that is desirable and useful to cause immune cells that are not selected on the basis of antigen specificity to express IL-10. The methods of the present claims differ from those disclosed in the '999 patent by accomplishing the expression of IL-10 by genetic modification as contrasted to using a stimulant to regulate expression of the endogenous gene.

6. Takayama *et al.* studied the influence of viral IL-10 and mammalian IL-10 gene transfer on the ability of dendritic cells to stimulate T-cells and natural killer (NK) cells and their impact on the growth of transplantable tumors. Myeloid DC progenitors were propagated from mouse bone marrow in granulocyte-macrophage colony-stimulating factor + IL-4, and the vIL-10 or mIL-10 genes were introduced by retroviral vectors (see Abstract). Thus, the method practiced by Takayama *et al.* differs from the method of claims 1-5 (the 'dendritic cell' embodiment in claim 3) only in using bone marrow, not peripheral blood, as the source of cells.

7. Setoguchi *et al.* teach the transfection of splenocytes with a retroviral vector encoding IL-10 (see p. 5981). Setoguchi *et al.* teach using T cells as vehicles for delivering useful agents (p. 5980, col. 2, 1st full paragraph) and further, that IL-10 is known to mediate immunosuppressive

effects predominantly through down-regulation of macrophage functions and inhibition of proinflammatory cytokines produced by Th1 cells, that IL-10 was shown to prevent disease expression and development in collagen-induced arthritis by i.p. injection of mouse IL-10, or an adenovirus murine IL-10 (p. 5980-1, bridging paragraph). The Setoguchi *et al.* studies were performed using mice that were transgenic for TCR specific for the OVA antigen that had been used in their model of experimentally induced arthritis. Thus, the Setoguchi *et al.* methods differ from the presently claimed method by including antigen-specific lymphocytes. The stated purpose of the Setoguchi *et al.* studies was use the antigen-specific T-cells to affect local delivery of IL-10 to the site of inflammation. One of skill in the art would recognize that Setoguchi *et al.* established the importance and efficacy of IL-10 in treatment of inflammatory disease, including arthritis, and additionally suggest the usefulness of using T cells in order to deliver therapeutic agents. Furthermore, Setoguchi *et al.* disclosed that retroviral IL-10 gene transfer could be achieved in antigen nonspecific splenocytes by cultivating the cells in phytohemagglutinin, as in instant claim 6 (p. 1591, *Infection of the retrovirus*).

8. Mavilio *et al.* teach retrovirus-mediated transfer of LNGFR cDNA into peripheral blood mononuclear cells, as well as myeloid and lymphoid cell lines (Abstract). Regarding claim 4, Mavilio *et al.* teach culturing the cells for 72 hours prior to viral infection. Regarding claim 5, Mavilio teach using PHA and IL-2, which are proliferating agents. Regarding claim 6, Mavilio teach culturing the cells with phytohemagglutinin (PHA). Regarding claim 7, Mavilio teach using flow cytometry to isolate retroviral transduced cells. Regarding claim 8, Mavilio teach lymphocytes. Regarding claims 20-21, Mavilio *et al.* teach the production of an enriched lymphocyte population, which includes B lymphocytes, T lymphocytes or CD4+ lymphocytes.

9. US 6540999, Takayama *et al.*, and Setoguchi *et al,* each teach that controlled expression of IL-10 can be successfully used to modulate immune responses. The '999 patent further teaches immune modulation by secretion of IL-10 from immune cells that are not selected on the basis of antigen specificity. This is also supported by Takayama *et al.*, as dendritic cells are not antigen-specific in their action. Takayama *et al.*, Setoguchi *et al,* and Mavilio *et al.* provide technical means for expressing IL-10 in any of the cell populations or subsets recited in the instant claims. Therefore, one of skill in the art would be motivated and expect success in expressing IL-10 in immune cells that are not selected on the basis of antigen specificity, including peripheral blood lymphocytes, and in using the modified cells to treat inflammatory diseases. Thus, the instantly claimed methods are *prima facie* obvious in view of the combined teachings of the cited references.

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C. Gamett, PhD., whose telephone number is (571)272-1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel C Gamett/
Examiner, Art Unit 1647